

09/83,745
allow² Claims
1 - 9

allowance

WHAT IS CLAIMED IS:

1. A method for selecting a clone of an ES cell containing a mutation in a gene that is expressed in a test cell comprising:
 - 5 (a) providing cDNA obtained by reverse transcription of mRNA of the test cell;
 - (b) providing a collection of cultured ES cells organized into individual clones, wherein each clone is of an ES cell having a mutation in an exon in its genome, the mutation being in a different exon in cells of different clones;
 - (c) providing an array of different single stranded polynucleotides, the polynucleotides being fragments of exons containing mutations in (b);
 - 10 (d) exposing the cDNA to the array under conditions permitting hybridization of polynucleotides in the array to nucleic acids;
 - (e) detecting hybridization of cDNA to a polynucleotide on the array; and,
 - 15 (f) selecting a clone in the collection from which a hybridizing polynucleotide detected at (c) is an exon fragment.
2. The method of claim 1, wherein the ES cells are murine.
3. The method of claim 1, wherein mutations in the ES cells are as a result of introducing an exon trap vector into ES cells.
- 20 4. The method of claim 1, wherein the array is a nucleic acid microarray.
5. The method of claim 4, wherein the microarray comprises at least 500 different polynucleotides on a solid support surface.
- 25 6. The method of claim 5, wherein the microarray comprises at least about 1,000 different polynucleotides.
- 30 7. The method of claim 1, wherein the cDNA is labelled to facilitate detection at (e).

8. The method of claim 7, wherein the label is fluorescent or radioactive.

9. The method of claim 1, wherein selecting a clone comprises physically segregating a
5 sample of ES cells from a selected clone.

10. A method for comparing gene expression between test cells, comprising:

(a) providing at least two cDNA samples, each sample obtained by reverse transcription of mRNA of a different test cell;

10 (b) providing a collection of cultured ES cells organized into individual clones,
wherein each clone is of an ES cell having a mutation in an exon of its genome, the mutation
being in a different exon in cells of different clones;

(c) providing at least one array of different single stranded polynucleotides, the
polynucleotides being fragments of exons containing mutations in (b);

15 (d) exposing the cDNA samples to the at least one array under conditions
permitting hybridization of polynucleotides on the array to nucleic acids;

(e) detecting hybridization of polynucleotides in the at least one array resulting
from exposure to cDNA;

(f) selecting clones in the collection from which hybridizing polynucleotides
20 detected at (e) are exon fragments; and,

(g) comparing a clone or clones which comprise exon fragments that hybridize to
one of the cDNA samples to a clone or clones which comprise exon fragments that hybridize to
another of the cDNA samples.

25 11. The method of claim 10, wherein the ES cells are murine.

12. The method of claim 10, wherein mutations in the ES cells are as a result of
introducing an exon trap vector into ES cells.

30 13. The method of claim 10, wherein the array is a nucleic acid microarray.